Osteoarthritis and Cartilage 19 (2011) 272–280

Osteoarthritis and Cartilage

Does high weight loss in older adults with knee osteoarthritis affect bone-on-bone joint loads and muscle forces during walking?

S.P. Messier †*, C. Legault ‡, R.F. Loeser §, S.J. Van Arsdale †, C. Davis ‡, W.H. Ettinger ||, P. DeVita ¶

† *J.B. Snow Biomechanics Laboratory, Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC, USA*
‡ *Department of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC, USA*
§ *Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA*
|| *Department of Medicine, University of Massachusetts Medical School, North Worcester, MA, USA*
¶ *Department of Exercise and Sport Science, East Carolina University, Greenville, NC, USA*

ARTICLE INFO

Article history:
Received 25 March 2010
Accepted 26 November 2010

Keywords:
Biomechanics
Gait
Knee joint loads
Musculoskeletal modeling
Knee OA

SUMMARY

Objective: The aim of this study was to examine the effects of high weight loss on knee joint loads during walking in participants with knee osteoarthritis (OA).
Design: Data were obtained from a subset of participants enrolled in the Arthritis, Diet, and Activity Promotion Trial (ADAPT). Complete baseline and 18-month follow-up data were obtained on 76 sedentary, overweight or obese older adults with radiographic knee OA. Three-dimensional gait analysis was used to calculate knee joint forces and moments. The cohort was divided into high (>5%), low (<5%), and no (0% or gain) weight loss groups.
Results: From baseline body weight, the high weight loss group lost an average of 10.2%, the low weight loss group lost an average of 2.7%, and the no weight loss group gained 1.5%. Adjusted 18-month outcome data revealed lower maximum knee compressive forces with greater weight loss ($P = 0.05$). The difference in compressive forces between the high weight loss and no weight loss groups was due primarily to lower hamstring forces ($P = 0.04$). Quadriceps forces were similar between the groups at 18-month follow-up. There was no difference between the groups in 18-month joint space width or Kellgren–Lawrence scores.
Conclusions: These results suggest that a 10% weight loss in an overweight and obese osteoarthritic population elicits positive changes in the mechanical pathway to knee OA by having lower knee joint compressive loads during walking compared to low and no weight loss groups. The difference in compressive forces was due, in large part, to reductions in hamstring co-contraction during the initial portion of the stance phase.

The most important *modifiable* risk factor for development and progression of knee osteoarthritis (OA) is obesity[1–8]. Weight loss reduces the risk of symptomatic knee OA[4] and may have important implications for mortality risk[9]. Weight loss combined with exercise is recommended for obese knee OA sufferers by both the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR)[10,11].

We have shown a significant and direct correlation between weight loss and attenuation of knee joint forces and moments during walking in this population[12]. A reduction of 1 lb in body weight was associated with a four times larger loss in knee joint compressive forces. This implies that the greater the intentional weight loss, the lower the stress on the knee, thereby enhancing the potential of slowing disease progression and improving clinical outcomes. Indeed, mechanical factors are implicated in the pathogenesis of knee OA, and obesity plays a role in this pathway by increasing joint loads[13]. As a result, there is increased tissue damage, cartilage loss, pain, and ultimately, disability.

Our previous work was limited to low-to-moderate weight loss. A moderate, 5% weight loss, when combined with exercise, improved function and pain but was not a sufficient stimulus to slow disease progression[14]. The purpose of this exploratory analysis was to use a selected subset from our previous study[14] (i.e., those with complete biomechanical observations) to expand the boundaries of weight loss to larger, potentially more clinically meaningful amounts to provide evidence whether high weight loss in older overweight and obese adults with knee OA consequent to

* Address correspondence and reprint requests to: Stephen P. Messier, J.B. Snow Biomechanics Laboratory, Department of Health & Exercise Science, Wake Forest University, Winston-Salem, NC 27109, USA.
E-mail address: messier@wfu.edu (S.P. Messier).

1063-4584/$ – see front matter © 2010 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.joca.2010.11.010

participation in an 18-month diet and exercise clinical trial reduces knee joint loads and attenuates disease progression relative to low weight loss, and no weight loss or weight gain.

Patients and methods

Design

ADAPT was a single-blind, randomized controlled clinical trial of overweight and obese sedentary older adults with symptomatic knee OA[14,15]. The study was designed to compare the effects of assignment to four distinct 18-month interventions: (1) exercise, (2) dietary weight loss (diet), (3) dietary weight loss plus exercise (diet-plus-exercise), and (4) healthy lifestyle (control). ADAPT was conducted at the Claude D. Pepper Older Americans Independence Center of Wake Forest University, with the approval of the university's institutional review board and in accordance with the Helsinki Declaration.

Participants

Sedentary, overweight and obese, older adults with radiographic evidence of knee OA were recruited in six waves over an 18-month period. Detailed inclusion and exclusion criteria are noted elsewhere[14,15]. Briefly, inclusion criteria included: (1) age ≥ 60 years; (2) overweight or obese (Body Mass Index (BMI) $\geq 28.0\ kg \times m^{-2}$); (3) radiographic evidence in one or both knees of Kellgren–Lawrence (KL) grades I–III tibio-femoral OA in weight-bearing anteroposterior view and/or patellofemoral OA in sunrise view; (4) no more than 20 min of regular exercise per week; (5) self-report of knee pain on most days of the month; (6) self-report of difficulty due to knee pain in one or more daily activities (e.g., walking one-quarter mile, shopping, bending, etc); and (7) willingness to undergo testing and intervention procedures. Exclusion criteria included: (1) serious co-morbid medical condition that could prevent safe participation in an exercise program; (2) score of <24 on Mini-Mental State Exam (MMSE); (3) inability or unwillingness to modify dietary and/or exercise behaviors; (4) inability to complete the 18-month study or probability of noncompliance; (5) inability to walk without a cane or other assistive device; (6) participation in another interventional research study; (7) self-reported alcohol consumption of >14 drinks/week; or (8) ST-segment depression of >2 mm at an exercise level of four METs or less, hypotension or complex arrhythmias during a graded exercise test[16].

A total of 316 individuals were randomized to one of the four treatment groups. A subset of this population ($n = 142$), equally represented in the four intervention groups, was randomized to ancillary biomechanics testing. The descriptive characteristics of the biomechanics subset were similar to those of the entire ADAPT cohort and are presented elsewhere[12] with a flowchart of participant progress. Testing was conducted at baseline, 6- and 18-month follow-up. For this study, only participants who had complete baseline and 18-month biomechanical data were included ($N = 76$). There was no significant difference ($P = 0.17$) in baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) function between the subset of participants with and without complete ancillary data. We compared participants who lost more than 5% of their baseline weight ($n = 24$) to those who lost less than 5% ($n = 23$), and who did not lose or gained weight ($n = 29$) at the end of 18 months. The following analyses include all 76 participants and group comparisons based on all participants, and on the 53 participants at the higher and lower end of the weight loss (gain) distribution.

Interventions

The exercise, diet, exercise-plus-diet, and healthy lifestyle interventions are described in detail elsewhere[14,15]. Participants randomized to either exercise or diet-plus-exercise interventions were prescribed a 3-days/week exercise regimen combining aerobic (walking) and resistance training. The 60-min workout consisted of a 15-min aerobic phase, a 15-min resistance training phase, a second 15-min aerobic phase, and a 15-min cool-down.

The dietary therapy intervention focused on reducing fat and total calories. Participants were taught to evaluate and to modify food intake, with less than 30% of calories derived from fat. The weight-loss goal was 5% of the participants' body weight.

The diet-plus-exercise group combined the therapy programs outlined above. The healthy lifestyle intervention served as the attention control group and provided social interaction and health education. Three monthly 1-h presentations on topics related to knee OA, obesity, and exercise were followed by monthly (months 4–6), then bimonthly (months 7–18) phone calls.

Prior to participation, the experimental procedures were explained to each participant and an informed consent document was signed.

Measurements and procedures

Gait analysis

Prior to testing at baseline and 18-month follow-up visits, participants' freely chosen walking speeds were assessed using a Lafayette Model 63501 photoelectric control system interfaced with a digital timer. The photocells were positioned 7.3 m apart on an elevated walkway. Participants traversed the 7.3 m course six times. Freely chosen walking speed was calculated as the mean of the six trials. This speed ($\pm 3.5\%$) was used in all subsequent gait evaluations for the particular test period.

To control for the effects of footwear, each participant wore an identical make and model athletic shoe during testing. Three-dimensional (3D) high-speed (60 Hz) videography was performed using a four-camera motion analysis system (Motion Analysis Corporation, Santa Rosa, CA). Raw coordinate data from the 3D system was smoothed using a Butterworth low-pass digital filter with a cut-off frequency of 6 Hz. Temporal and lower extremity kinematic and kinetic variables were computed using Orthotrak software and an Advanced Mechanical Technologies Inc (AMTI) model SGA6-4 force platform (AMTI, Watertown, MA) set to sample data at 1000 Hz. Three successful trials, in which the participant walked within $\pm 3.5\%$ of freely chosen speed and placed the entire foot on the force platform in a visually normal stride, were averaged to yield representative values. Kinematic and kinetic data were synchronized, which allowed calculation of net joint forces and moments at the lower extremity joints through standard inverse dynamic techniques (e.g., Winter[17]). A biomechanical model was subsequently used to calculate knee muscle and joint forces from the net joint forces and moments, the kinematic data, and related anatomical and physiological characteristics. The model is described in detail in the Appendix. The outcomes were the peak values of seven knee joint kinetic variables: compressive and anteroposterior shear forces, hamstrings, quadriceps and gastrocnemius forces, the internal knee extension and abduction moments.

Knee radiographs

Bilateral anteroposterior weight-bearing knee radiographs were used to assess the presence of tibiofemoral arthritis, and bilateral sunrise views were used to assess the presence of patellofemoral arthritis. Both radiographs were obtained at baseline and 18 months. The weight-bearing radiographs were obtained with the participant's knees flexed at a 15° angle. The X-ray beam was centered on the joint space. Foot maps were used at baseline and follow-up to assure similar positioning for the two radiographs. The focus-to-film distance was held constant throughout the study.

A single physician blinded to the treatment group read the radiographs paired for each subject. Severity of tibiofemoral OA was determined using the KL grading scale (0 = no disease; 1 = questionable; 2 = definite; 3 = moderate; 4 = severe)[18]. Medial and lateral joint space widths were measured by determining the smallest distances between the cortical margins of the tibia and femur for each compartment using a 10× magnifying lens and a 0.1 mm graded ruler.

Statistical analysis

Statistical analyses were performed using SAS. Three weight loss groups were created: more than 5% weight loss at the end of 18 months (High), 0.1–5% weight loss (Low), and no change or weight gain (No). Fischer's exact test revealed that the allocation of subjects to the three weight classifications was not dependent on intervention group assignment ($P = 0.29$). Baseline analyses included descriptive statistics consisting of frequency tables and percents for categorical variables and means and standard deviations (SDs) for continuous variables. Bivariate plots were used to describe associations between weight loss and outcomes. Analysis of covariance was used to obtain estimates of weight loss effects at 18-month follow-up adjusting for pre-randomization levels of the baseline value of the outcome being analyzed, age, gender, walk speed and ADAPT intervention. Models include all 3 groups, overall *P*-value, and the *P*-value comparing the high weight loss group to the group with no change or weight gain. Corresponding 18-month change is reported from models with change as the dependent variable and the same independent variables as described above. Percent change is obtained by dividing the change by the baseline mean. These analyses were conducted at the 0.05 two-sided level of significance.

Results

Retention

Of the 142 participants randomized to biomechanics testing, 116 (82%) had complete data for at least one follow-up biomechanical visit (at 6 and/or 18 months). Only participants who had complete baseline and 18-month biomechanical and weight loss data were included ($N = 76$). The proportion of participants that completed ancillary biomechanics 18-month testing was lower than the completion rate for the primary outcome of the entire ADAPT cohort (80%). This was due, in large part, to the additional burden placed on these participants that included both biomechanics and strength testing. There was no significant difference ($P = 0.17$) in baseline WOMAC function between those who completed the biomechanics testing (23.8 ± 1.28) and those who did not (26.6 ± 1.55).

Weight loss

Baseline and 18-month follow-up values for body weight are shown in Table I. Baseline weight ranged from 70 kg to 148 kg in the high weight loss group, from 69 kg to 118 kg in the low weight loss group, and from 67 kg to 117 kg in the no weight loss group. The high weight loss group lost an average of 10.2% (9.5 kg) of baseline body weight, the low weight loss group lost 2.7% (2.5 kg), and the no weight loss group gained 1.5% (1.3 kg).

Walking velocity

Baseline walking velocities were similar between the high weight loss ($1.17 \pm 0.04\ ms^{-1}$), low weight loss ($1.21 \pm 0.04\ ms^{-1}$) and no weight loss ($1.20 \pm 0.04\ ms^{-1}$) groups. These groups increased walking velocity by 6.8% ($1.25 \pm 0.04\ ms^{-1}$), 7.4% ($1.30 \pm 0.04\ ms^{-1}$) and 4.2% ($1.25 \pm 0.04\ ms^{-1}$), respectively, across the 18-month intervention. There was no significant ($P = 0.59$) between-group difference at 18-month follow-up. The increase over the 18-month intervention period was significant in the high and low weight loss groups ($P = 0.04$ and 0.003, respectively), but not in the no weight loss group ($P = 0.38$).

Knee joint loads

Adjusted 18-month outcome data revealed lower maximum knee compressive forces with greater weight loss ($P = 0.05$) (Table II). This was due, in part, to the significantly lower vertical ground reaction forces ($P = 0.003$). In contrast, there were no differences in AP shear forces between the groups. Internal knee abduction moment, a surrogate measure of knee joint load in previous studies, is an important component of the knee compression force. The 18-month abduction moment values were slightly lower in the high weight loss group compared to the low and no weight loss groups, however, the differences were not significant. There was no difference in peak extension moments between the groups over 18 months (Table II).

Maximum hamstring force was significantly different ($P \leq 0.03$) among the 3 groups, with the high weight loss group having lower values than both the low and no weight loss groups (Table III). Quadriceps forces were similar between the groups at 18-month follow-up. All groups increased quadriceps force from baseline. Gastrocnemius peak forces showed a non-significant dose response trend with greater weight loss resulting in lower forces. The greatest difference in these forces was between the high and the no weight loss groups ($P = 0.10$, ES = 0.45) (Table III).

Radiographic progression

KL scores on the most affected knee at 18-month follow-up, adjusted for baseline KL differences, were not statistically different between the groups ($P = 0.44$) (Table IV). In addition, there were no between-group differences in medial or later joint space widths.

Discussion

In our musculoskeletal model, the quadriceps, hamstrings, and gastrocnemius muscle forces account for a major portion of the knee compressive and shear forces as in other studies[19–21]. Hence, any change in compressive or shear forces will be due, in large part,

Table I
Mean (95% CI) weight and weight loss values at baseline and 18 months follow-up for the high, low, and no weight loss groups

Weight loss	N	Baseline weight (kg)	18-month weight (kg)	Change in weight (kg)	%Δ
High	24	93.0 (85.9; 100.0)	83.4 (76.9; 90.0)	−9.5 (−11.9; −7.1)	−10.2 (−12.3; −8.0)
Low	23	89.7 (83.6; 95.7)	87.2 (81.4; 92.9)	−2.5 (−3.1; −1.9)	−2.7 (−3.3; −2.2)
No	29	94.8 (90.2; 99.4)	96.2 (91.7; 100.6)	1.3 (0.7; 2.0)	1.5 (0.8; 2.2)

Weight loss: high = −27% to −5.1 %, low = −5% to −0.01%, none = 0% to 7.5%
CI = Confidence Interval

Table II
Comparison of maximum knee joint loads (mean ± 95% CI) by weight loss group at 18-month follow-up, after adjusting for age, gender, walk speed, ADAPT intervention and baseline value

Variable	Weight loss	Baseline	Adjusted 18-month	*P*-value Overall (High vs No)	Δ	% Δ
AP shear force (N)	High	461 (377; 545)	585 (481; 689)	0.61 (0.44)	107.8	23.4
	Low	453 (373; 533)	514 (404; 625)		37.5	8.3
	No	512 (464; 559)	529 (429; 630)		52.4	10.2
Compressive force (N)	High	2852 (2433; 3271)	2843 (2573; 3114)	0.05 (0.01)	−75.2	−2.6
	Low	2908 (2628; 3188)	3049 (2755; 3342)		130.1	4.5
	No	2969 (2678; 3261)	3310 (3050; 3570)		391.3	13.2
Abduction moment (Nm)	High	38 (32; 44)	34 (28; 40)	0.65 (0.44)	−2.8	−7.4
	Low	37 (30; 45)	37 (31; 43)		0.7	1.9
	No	34 (29; 40)	37 (31; 49)		0.2	0.6
Extension moment (Nm)	High	33 (21; 46)	34 (25; 43)	0.21 (0.72)	−0.9	−2.7
	Low	41 (24; 58)	23 (13; 33)		−12.4	−30.3
	No	32 (25; 39)	32 (23; 40)		−3.3	−10.4
Vertical ground reaction force (N)	High	976 (860; 1092)	892 (830; 953)	0.003 (0.001)	−135.7	−13.9
	Low	1118 (721; 1514)	949 (886; 1012)		−78.6	−7.0
	No	993 (945; 1041)	1036 (983; 1089)		8.2	0.8

Weight loss: high = −27% to −5.1 %, low = −5% to −0.01%, none = 0 to 7.5%, Δ = mean at month 18 − mean at baseline, % Δ = Δ/mean at baseline.
CI = Confidence Interval.

to changes in one of more of these muscle forces. Although quadriceps forces increased between 9% and 18% across the groups, the high weight loss group maintained peak knee compressive forces at baseline values, in part by reducing hamstring forces by 11%. This did not occur in the low and no weight loss groups, resulting in greater peak knee compressive forces relative to the high weight loss group. We presume the reduction in hamstring and knee compressive forces in the high weight loss group were caused by the reduced total body weight, thereby decreasing the amount of muscle force required to support and propel the subjects. Since walk speed can also influence knee joint forces and moments, we adjusted for group differences in our analyses. We do note however, the beneficial effect weight loss seemed to have on self-selected walking speed; i.e., the low and high weight loss groups increased walking speed ~7%. Himann *et al.*[22] noted that walk speed declined 1–2% per decade of life until age 63 years, when the decline per decade increased to 12.4% for females and 16.1% for males. Hence, the *increase* in walking speed in our older adult cohort suggests a slowing in the decline in mobility associated with aging and knee OA consequent to long-term weight loss and/or exercise interventions.

Intuitively, a reduction in body weight would lower the vertical ground reaction forces. A mean weight loss exceeding 10% in the high weight loss group resulted in lower peak vertical ground reaction loads. Interestingly, these changes did not exactly coincide with the changes observed in the knee compressive forces. Most notably, the vertical ground reaction force was reduced after 18 months in the low weight loss group, but the knee joint compressive force was actually increased from baseline to 18-month follow-up. We suggest, therefore, that while the external ground reaction force provides an approximation of joint loads, observed changes over time may not be indicative of the actual changes occurring within the joint.

Figure 1 shows the timing of peak compressive, quadriceps, hamstring, and gastrocnemius forces during gait. The period of greatest challenge for an older adult with knee OA occurs shortly after heel strike during weight acceptance[23]. As shown through electromyographic data, the quadriceps and the hamstrings contract simultaneously (i.e., co-contract) to help stabilize the knee during this challenging load bearing period, and this co-contraction is increased in knee OA patients[24–26]. The hamstrings also lessen the anterior shear force caused by the quadriceps, and control hip extension throughout stance. The more co-contraction, however, the greater the compressive forces exerted on the knee. Within the limitations of our muscle force predictions (see Appendix below), our data enable us to uniquely estimate co-contraction through the relationship of actual muscle forces instead of muscle activation patterns. These data suggest that with greater weight loss, osteoarthritic patients were able to reduce the level of co-contraction by reducing hamstrings but not quadriceps force, thereby limiting the compressive load exerted on the knee. Indeed, there was a significant dose response to weight loss, with the high weight loss group having significantly lower peak knee compressive forces relative to the low and no weight loss groups at 18-month follow-up.

The gastrocnemius, as part of the triceps surae complex, acts primarily to stabilize the ankle, restrain the rate of tibial advancement throughout stance, and provide force at push off to support and propel body mass[23,27]. Gastrocnemius forces peak during terminal stance[20,28,29] and, therefore, have more influence on the magnitude of the second peak knee compressive force (see Fig. 1).

Table III
Comparison of maximum muscle forces (mean ± 95% CI) by weight loss group predicted from the musculoskeletal model at 18-month follow-up, after adjusting for age, gender, walk speed, ADAPT intervention and baseline value

Variable	Weight Loss	Baseline	Adjusted 18-month	*P*-value Overall (High vs No)	Δ	% Δ
Gastrocnemius force (N)	High	673 (619; 728)	595 (502; 688)	0.19 (0.10)	−95.5	−14.2
	Low	657 (604; 711)	695 (595; 795)		4.7	0.7
	No	746 (693; 799)	703 (612; 796)		−13.1	−1.8
Hamstring force (N)	High	799 (665; 933)	697 (607; 787)	0.03 (0.04)	−88.4	−11.1
	Low	754 (644; 864)	864 (765; 963)		78.9	10.5
	No	821 (713; 930)	822 (738; 906)		36.7	4.5
Quadriceps force (N)	High	1292 (941; 1642)	1460 (1165; 1754)	0.84 (0.76)	179.5	13.9
	Low	1258 (1022; 1494)	1396 (1080; 1712)		116.1	9.2
	No	1340 (1136; 1545)	1520 (1240; 1799)		239.6	17.9

CI = Confidence Interval.

Table IV
Comparison of joint space width (mm) and K–L score (mean ± 95% CI) at baseline and 18-month follow-up by weight loss group, after adjusting for age, gender, walk speed, ADAPT intervention and baseline value

Variable	Weight loss	Baseline	Adjusted 18-month	*P*-value Overall (High vs No)	Δ	% Δ
Lateral joint space width (mm)	High	4.56 (3.82; 5.30)	4.35 (3.89; 4.81)	0.46 (0.50)	−0.137	−3.0
	Low	4.40 (3.75; 5.04)	4.50 (4.08; 4.92)		0.009	0.2
	No	4.38 (3.69; 5.08)	4.16 (3.79; 4.53)		−0.332	−7.6
Medial joint space width (mm)	High	3.17 (2.64; 3.69)	3.12 (2.88; 3.36)	0.67 (0.41)	−0.120	−2.6
	Low	2.99 (2.21; 3.76)	3.00 (2.76; 3.25)		−0.240	−4.5
	No	3.47 (3.00; 3.93)	2.99 (2.77; 3.20)		−0.256	−13.2
KL score	High	2.36 (1.92; 2.79)	2.47 (2.30; 2.63)	0.44 (0.37)	0.149	6.3
	Low	2.39 (1.98; 2.79)	2.61 (2.45; 2.77)		0.293	12.3
	No	2.26 (1.97; 2.55)	2.56 (2.42; 2.70)		0.244	10.8

Taken together, the lower peak forces in the knee flexors and, to a lesser extent, the ankle plantar flexors among the high weight loss participants suggest that the greater weight loss resulted in less co-contraction for knee stabilization and reduced force requirements for ankle stabilization, tibial advancement, and push off.

The high weight loss group had significantly lower knee compressive forces and was the only cohort that reduced the internal knee abduction moment, a surrogate measure of knee joint loading, from baseline to follow-up. Reduced knee joint loading through intense weight loss may play a role in slowing disease progression by eliciting positive changes in the mechanical pathway to knee OA. These mechanical improvements, however, did not result in concomitant changes in disease progression. Radiography is relatively insensitive to change and does not evaluate disease in soft tissue structures. A larger sample size, the use of a more sensitive measure of progression, such as Magnetic Resonance Imaging (MRI), or a longer intervention period (i.e., the effect that weight loss has on progression may be evident sometime later) may have enhanced our ability to detect differences in progression among the groups.

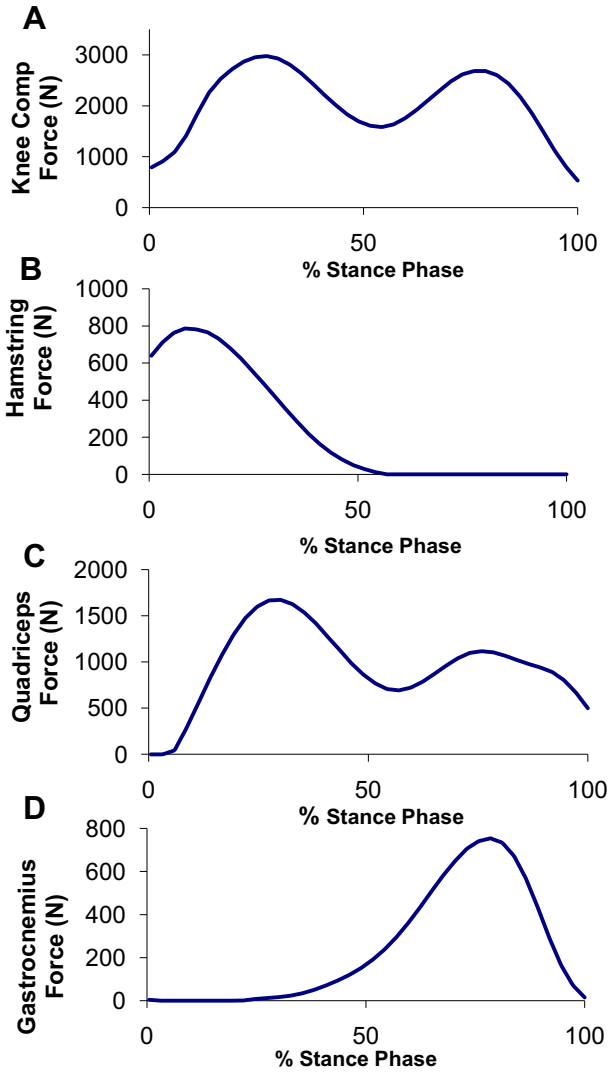

Fig. 1. (A) Knee compressive, and (B) Hamstring, (C) Quadriceps, and (D) Gastrocnemius muscle forces of a complete stance phase of a typical participant. Note: 1 body weight = 923.1 N (94.1 kg).

Our previous study of dietary therapy and its effect on gait in people afflicted with knee OA was limited to moderate weight loss[12]. We expanded the boundaries of weight loss to larger, potentially more clinically meaningful amounts and found that higher weight loss than previously studied elicited beneficial effects. Specifically, high weight loss (mean = 10.2%) resulted in lower knee joint compressive loads relative to low and no weight loss or weight gain, primarily by reducing hamstring co-contraction during the initial portion of the stance phase.

The importance of the aggressive use of non-pharmacologic co-therapies such as intensive weight loss for improving symptoms associated with OA, slowing disease progression, and impacting the underlying mechanisms of OA is under appreciated. Our study provides evidence that intensive long-term weight loss affords biomechanical improvements in knee joint loads not seen in low or no weight loss groups. Future study of long-term high intensity weight loss as a possible OA disease modifying intervention is needed using more sensitive measures of disease progression. The potential benefits of intensive weight loss for co-morbidities common to obese, knee OA patients such as heart disease, stroke, and type II diabetes enhance further the import of this non-pharmacologic intervention.

Author contributions

Each author made the following contributions to this manuscript: conception and design (SPM, CL, SJV, PD), analysis, interpretation of the data, critical revision, final approval (SPM, CL, RFL, SJV, CD, WHE, PD), statistical expertise (CL, CD), funding (SPM, WHE), and data collection (SPM, SJV).

Conflicts of interest

The authors have no conflicts of interest.

Acknowledgements

The authors would like to acknowledge the contributions of Jovita Jolla Newman and Shubham Khajanchi, research technicians, who assisted in data collection. This study was supported by NIH grants 5P60-AG-10484-07 and M01-RR-0021.

Appendix. Biomechanical knee model

We used a biomechanical model of the knee to calculate total compressive and anterior–posterior shear forces within the tibio-femoral compartment of the knee joint. The model (see Fig. 2) used lower extremity joint forces and moments calculated with inverse dynamics along with the kinematics of the lower extremity and related anatomical and physiological characteristics to calculate forces in the three largest knee muscles and in the lateral soft tissue support structures (e.g., lateral collateral ligament). These forces were combined with the knee joint reaction forces to determine the tibio-femoral compressive and shear forces[30,31]. Gastrocnemius force was determined from the plantar flexor moment during the stance phase of gait. It was assumed that this moment was produced by triceps surae muscles (gastrocnemius and soleus). Triceps surae force was calculated as the quotient of the plantar flexor moment and the moment arm for the triceps surae at the observed angular position of the ankle. Muscle moment arm values for each ankle position were derived from moment arm–ankle joint position curves from the literature[30,31]. The mean value throughout the ankle Range of Motion (ROM) for the moment arm was 0.051 m. Gastrocnemius force was then partitioned from triceps surae force based on its proportion of the total physiological cross sectional area (PCA) of the triceps surae which was 0.319[32]. These methods were supported by the strong association between gastrocnemius Electromyography (EMG) and ankle plantar flexor torque[33–36] and in directly measured force in the Achilles tendon during walking[37,38]. The direction of the gastrocnemius force was determined from the heel and knee marker positions. The heel marker represented the distal end of the gastrocnemius. The proximal end was positioned 0.020 m superior and 0.023 m posterior to the knee joint, along the line of the femur[39]. The resultant direction of the gastrocnemius force was ~3° from parallel with the leg and applied a relatively large compressive load but small shear load on the knee.

Hamstrings force was calculated from the extensor moment at the hip observed typically during the first half of stance. This method was supported by the strong association between hip extensor moment and hamstrings EMG in early stance[34,36,40]. The hip extensor moment was assumed to be produced by the hamstrings and gluteus maximus muscles and it was assumed that there was no co-contraction of the hip flexors during the first half of stance. This assumption was generally supported by EMG measures and muscle force predictions in the literature except that rectus femoris does partially contract and produce force during some of this period[40,41]. The predicted hamstrings force accounted for both the hamstrings PCA relative to the total PCA of the hamstrings and gluteus maximus and the hamstrings moment arm at the hip relative to the gluteus maximus moment arm. The total hamstrings proportion to the hip moment were calculated as:

$$\mathrm{Hp} = (\mathrm{Ham\ PCA}/(\mathrm{Ham\ PCA} + \mathrm{GM\ PCA}))(\mathrm{Hd}/\mathrm{GMd}) \quad (1)$$

where Hp is the proportion of the hip extensor moment generated by the hamstrings, Ham PCA and GM PCA were the hamstrings and gluteus maximus PCAs, and Hd and GMd are the hamstrings and gluteus maximus moment arms. Values for each of these constants were obtained from the literature[32,42] and were: Ham PCA = 42.4 mm^2, GM PCA = 17.36 mm^2, Hd = 0.042 m, and GM d = 0.047 m. The proportion of the hip extensor moment generated by the hamstrings (Hp) was equal to 0.63 of the total moment. The hamstrings force was then calculated as:

$$H = \mathrm{Hp}(\mathrm{Het})/\mathrm{Hd} \quad (2)$$

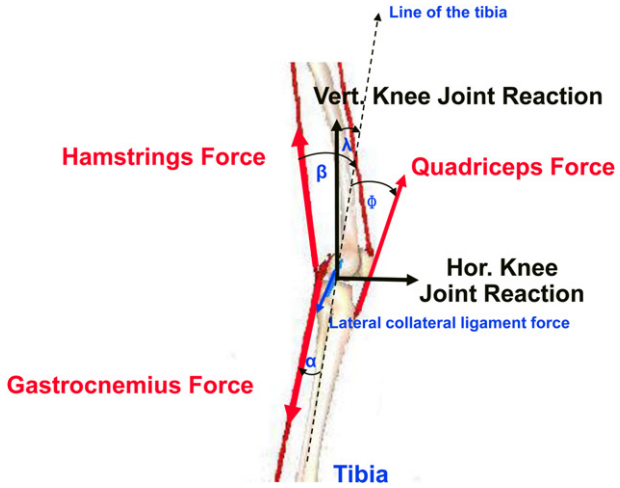

Fig. 2. Schematic representation of the biomechanical musculoskeletal knee model used to calculate knee joint loads and muscle forces (see Appendix for details).

where H was the hamstrings force and Het was the hip extensor moment. Hamstrings force was assumed to be zero when the hip torque was in the flexor direction typically during the second half of stance which is supported by hamstring EMG data[24,36,43]. The hamstrings force was directed parallel to the femur.

The quadriceps force were calculated from the observed net knee joint torque and the hamstrings and gastrocnemius forces and thereby accounted for co-contracting knee flexors. The observed net knee torque was a function of all muscles crossing the joint:

$$\mathrm{Kt} = Q(\mathrm{Qd}) - H(\mathrm{Hd}) - G(\mathrm{Gd}) \quad (3)$$

where Kt was the net knee torque from inverse dynamics, Q, H, and G were the forces by the quadriceps, hamstrings and gastrocnemius muscles, and Qd, Hd, and Gd were the respective moment arms for the muscles at the knee based on the observed knee angular positions. The force in the quadriceps, Q, was then calculated as:

$$Q = (\mathrm{Kt} + \mathrm{H}(\mathrm{Hd}) + \mathrm{G}(\mathrm{Gd}))/\mathrm{Qd} \quad (4)$$

Moment arms at the knee were obtained from the literature by averaging the values from a number of studies and for each angular position of the knee joint[31,44–47]. The mean values throughout the knee ROM for the three moment arms were, Qd = 0.035 m, Hd = 0.032 m, and Gd = 0.018 m. The direction of Q was determined from the literature[44,47] and was a function of knee angle.

The methods of Schipplein *et al.*[48] were used to determine the distribution of frontal plane loads and in particular the force in the lateral support structures at the knee during the stance phase. The external loads placed an adductor moment on the knee that was resisted by a combination of abductor moments from the quadriceps and the lateral structures. The quadriceps abductor moment (product of the quadriceps force and its frontal plane lever arm) was subtracted from the observed net internal abductor moment calculated by inverse dynamics. The remaining moment was distributed to the lateral knee tissues and the force in these tissues was calculated as the quotient of this torque and its moment arm. This force was considered to act parallel with the line of the tibia.

The final step was the calculation of knee joint forces. All muscle forces, the force in the lateral support structures and the joint reaction forces identified with inverse dynamics were partitioned into their compressive (parallel with the tibia) and anteroposterior shear (perpendicular to the tibia in the sagittal plane) components and summed. The equations were:

$$Ks = Gsin\,\alpha - Hsin\,\beta + Qsin\,\phi - Kzsin\,\lambda + Kycos\,\lambda \quad (5)$$

$$Kc = Gcos\,\alpha + Hcos\,\beta + Qcos\,\phi - Kzcos\,\lambda + Kysin\,\lambda + Lss \quad (6)$$

where Ks and Kc are the shear and compressive forces at the knee, Kz and Ky were the vertical and horizontal knee joint reaction forces, and Lss was the force in the lateral support structures. Ks was positive when the shear force applied an anterior load to the tibia and Kc was positive when the compressive force pushed into the tibia.

Limitations of biomechanical knee model

One limitation was the absence of several knee ligaments. The absence of cruciate and medial collateral ligaments increased the knee muscle force predictions since these tissues must resist some of the external loads. However, we expected that total knee loads were not severely affected because they were produced by the sum of all tissues crossing the joint regardless of whether these tissues are muscle or ligament. The model included the lateral support tissues (e.g., collateral ligament) which is important and produced the principle, non-muscular restraint during the stance phase of walking.

A second limitation was the assumption of no co-contraction by the hip flexors and the hip abductors during stance. The assumption of no co-contraction at the hip introduced some error due to missing force production in the rectus femoris which also applied force at the knee and the gluteus medius. This issue was relevant during the initial part of the stance phase when the hamstrings were active and produced force. These missing forces would tend to have opposite effects on hamstrings force (rectus femoris would increase and gluteus medius would decrease hamstrings force). Also, force in the rectus femoris during the first half of stance and relative EMG activation of this muscle are relatively low or even absent[28,49]. We therefore propose that our error in hamstrings force was relatively low. We performed a sensitivity analysis of the effect of hamstring error on knee force predictions. An underestimate of hamstrings force by 25% produced only a 5% error on knee force predictions.

A third limitation is that our model is a, "lumped muscle model," and cannot distinguish muscle forces between smaller muscle anatomical units. For example, we cannot uniquely identify Vasti from rectus femoris forces or medial from lateral Vasti muscles. Recent evidence showed that knee-OA patients have adaptations in medial and lateral Vasti muscle electromyographic patterns[25,50]. Our model however cannot identify underlying muscle forces associated with these activation changes. Also, our model cannot partition knee joint forces into lateral and medial compartment loads (as in[20,28]). This limitation most likely led to a partial underestimation of the knee compressive force.

Finally, our model may have underestimated the knee muscle forces because it was limited to satisfying the condition of static equilibrium but did not account for additional muscle forces due to increased muscle activation in OA patients e.g.,[25,26] This limitation may have also led to slightly underestimating the total knee compressive force. Overall, the combined limitations may have produced an underestimation of knee joint forces and this may explain the difference between the range of peak compressive forces (3.2 BW–3.7 BW) in our current and previous studies[12,43] and the value (4.3 BW) recently reported by Richards and Higginson[21]. When compared to a number of recent studies, our values are well within the range of values reported.

Table V
Comparison of peak muscle forces from Fig. 1 and previous studies

Muscle force	Present	Winby *et al.*	Wu *et al.*
Hamstrings force (N)	790	995	975
Quadriceps force (N)	1650	1600	2100
Gastrocnemius force (N)	780	1000	1480

Comparison of muscle and joint forces with other models

Our muscle force curves were similar in shape to those of Winby *et al.*[20] and Wu *et al.*[51]. Maximum hamstrings, quadriceps, and gastrocnemius forces occurred at approximately 12%, 25%, and 80% of the stance phase in each model. Muscle force predictions varied among the models. Using our representative subject (Fig. 1), present maximum hamstrings force was 20% less than reported in the other models, quadriceps force were within 3% of the value reported by Winby *et al.*, and our gastrocnemius force was more similar to the value reported by Winby *et al.* than was the value from Wu *et al.* (see Table V).

Except for the gastrocnemius force in Wu *et al.*, all other values were within 30% of one another and should be considered reasonably similar considering that differences among the tested populations in age, health status, and physical characteristics, along with differences in walking speeds could readily account for differences of this magnitude.

Predicted knee joint compressive forces were highly similar among several models including the present model. All models showed biphasic force curves with maximum values at approximately 30% and 80% of the stance phase. Our maximum force prediction was 24% higher than those by Kim *et al.* and Lin *et al.* and was 16% lower than the prediction by Winby *et al.* Our prediction was also within the 1 SD range reported in the Winby study and nearly identical to the value reported by Taylor *et al.* of 3.2 BW.

It appears from the muscle and joint force comparisons that our modeling procedures produce results as acceptable and as accurate as those from other biomechanical models.

References

1. Davis MA, Ettinger WH, Neuhaus JM. Obesity and osteoarthritis of the knee: evidence from the National Health and Nutrition Examination Survey (NHANES I). Semin Arthritis Rheum 1990 Dec;20(3 Suppl 1):34–41.
2. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. Ann Intern Med 1988 Jul 1;109(1):18–24.
3. Felson DT. The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. Semin Arthritis Rheum 1990 Dec;20(3 Suppl 1):42–50.
4. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. Ann Intern Med 1992 Apr 1;116(7):535–9.
5. Hartz AJ, Fischer ME, Bril G, Kelber S, Rupley Jr D, Oken B, *et al.* The association of obesity with joint pain and osteoarthritis in the HANES data. J Chronic Dis 1986;39(4):311–9.
6. Hochberg MC, Lethbridge-Cejku M, Scott Jr WW, Reichle R, Plato CC, Tobin JD. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: data from the Baltimore Longitudinal Study of Aging. J Rheumatol 1995 Mar;22(3):488–93.
7. Spector TD, Hart DJ, Doyle DV. Incidence and progression of osteoarthritis in women with unilateral knee disease in the

general population: the effect of obesity. Ann Rheum Dis 1994 Sep;53(9):565–8.
8. Sturmer T, Gunther KP, Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study. J Clin Epidemiol 2000 Mar 1;53(3):307–13.
9. Shea MK, Houston DK, Nicklas BJ, Messier SP, Davis CC, Miller ME, *et al*. The effect of randomization to weight-loss on total mortality in older overweight and obese adults: the ADAPT study. J Gerontol Med Sci 2010;65A:519–25.
10. Pendleton A, Arden N, Dougados M, Doherty M, Bannwarth B, Bijlsma JW. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including therapeutic trials (ESCISIT). Ann Rheum Dis 2000;59:936–44.
11. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000 Sep;43(9):1905–15.
12. Messier SP, Gutekunst DJ, Davis C, Devita P. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. Arthritis Rheum 2005 Jul;52(7):2026–32.
13. Griffin TM, Guilak F. The role of mechanical loading in the onset and progression of osteoarthritis. Exerc Sport Sci Rev 2005 Oct;33(4):195–200.
14. Messier SP, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, *et al*. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. Arthritis Rheum 2004 May;50(5):1501–10.
15. Miller GD, Rejeski WJ, Williamson JD, Morgan T, Sevick MA, Loeser RF, *et al*. The Arthritis, Diet and Activity Promotion Trial (ADAPT): design, rationale, and baseline results. Control Clin Trials 2003 Aug;24(4):462–80.
16. Berry MJ, Brubaker PH, O'Toole ML, Rejeski WJ, Soberman J, Ribisl PM. Estimation of VO2 in older individuals with osteoarthritis of the knee and cardiovascular disease. Med Sci Sports Exerc 1996;28:808–14.
17. Winter DA. Overall principle of lower limb support during stance phase of gait. J Biomech 1980;13(11):923–7.
18. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957 Dec;16(4):494–502.
19. Devita P, Lassiter Jr T, Hortobagyi T, Torry M. Functional knee brace effects during walking in patients with anterior cruciate ligament reconstruction. Am J Sports Med 1998 Nov;26(6):778–84.
20. Winby CR, Lloyd DG, Besier TF, Kirk TB. Muscle and external load contribution to knee joint contact loads during normal gait. J Biomech 2009 Oct 16;42(14):2294–300.
21. Richards C, Higginson JS. Knee contact force in subjects with symmetrical OA grades: differences between OA severities. J Biomech 2010 Sep 17;43(13):2595–600.
22. Himann JE, Cunningham DA, Rechnitzer PA, Paterson DH. Age-related changes in speed of walking. Med Sci Sports Exerc 1988 Apr;20(2):161–6.
23. Perry J. Gait analysis: normal and pathological function. Thorofare, NJ: Slack Inc; 1992.
24. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. Clin Biomech 2004 Jan;19(1):44–9.
25. Heiden TL, Lloyd DG, Ackland TR. Knee joint kinematics, kinetics and muscle co-contraction in knee osteoarthritis patient gait. Clin Biomech (Bristol, Avon) 2009 Dec;24(10):833–41.
26. Zeni JA, Rudolph K, Higginson JS. Alterations in quadriceps and hamstrings coordination in persons with medial compartment knee osteoarthritis. J Electromyogr Kinesiol 2010 Feb;20(1):148–54.
27. Neptune RR, Kautz SA, Zajac FE. Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking. J Biomech 2001 Nov;34(11):1387–98.
28. Lin YC, Walter JP, Banks SA, Pandy MG, Fregly BJ. Simultaneous prediction of muscle and contact forces in the knee during gait. J Biomech 2010 Mar 22;43(5):945–52.
29. Kim HJ, Fernandez JW, Akbarshahi M, Walter JP, Fregly BJ, Pandy MG. Evaluation of predicted knee-joint muscle forces during gait using an instrumented knee implant. J Orthop Res 2009 Oct;27(10):1326–31.
30. Rugg SG, Gregor RJ, Mandelbaum BR, Chiu L. In vivo moment arm calculations at the ankle using magnetic resonance imaging (MRI). J Biomech 1990;23(5):495–501.
31. Spoor CW, van Leeuwen JL. Knee muscle moment arms from MRI and from tendon travel. J Biomech 1992 Feb;25(2):201–6.
32. Yamaguchi GT, Sawa A, Moran D, Fessler M, Winters J. A survey of human musculotendon actuator parameters. In: Winters JM, Woo SL-Y, Eds. Multiple muscle systems. New York: Springer-Verlag; 1990:717–73.
33. Simonsen EP, Dyhre-Poulsen P, Voigt M, Aagaard P, Sjogaard G, Bojsen-Moller F. Bone on bone forces during loaded and unloaded walking. Acta Anatomy 1995;152:133–42.
34. Simonsen EB, Dyhre-Poulsen P, Voigt M, Aagaard P, Fallentin N. Mechanisms contributing to different joint moments observed during human walking. Scand J Med Sci Sports 1997 Feb;7(1):1–13.
35. Winter DA. Biomechanics of normal and pathological gait: implications for understanding human locomotor control. J Mot Behav 1989 Dec;21(4):337–55.
36. Winter DA, Yack HJ. EMG profiles during normal human walking: stride-to-stride and inter-subject variability. Electroencephalogr Clin Neurophysiol 1987;67:402–11.
37. Finni T, Komi PV, Lukkariniemi J. Achilles tendon loading during walking: application of a novel optic fiber technique. Eur J Appl Physiol Occup Physiol 1998 Feb;77(3):289–91.
38. Fukashiro S, Komi PV. Joint moment and mechanical power flow of the lower limb during vertical jump. Int J Sports Med 1987 Mar;8(Suppl 1):15–21.
39. Seireg A, Arvikar RJ. A mathematical model for evaluation of forces in lower extremities of the musculo-skeletal system. J Biomech 1973;6:313–26.
40. Shiavi R, Bugle HJ, Limbird T. Electromyographic gait assessment, Part 1: adult EMG profiles and walking speed. J Rehabil Res Dev 1987;24(2):13–23.
41. Andersson EA, Nilsson J, Thorstensson A. Intramuscular EMG from the hip flexor muscles during human locomotion. Acta Physiol Scand 1997 Nov;161(3):361–70.
42. Duda GN, Brand D, Freitag S, Lierse W, Schneider E. Variability of femoral muscle attachments. J Biomech 1996 Sep;29(9):1185–90.
43. Messier SP, Devita P, Cowan RE, Seay J, Young HC, Marsh AP. Do older adults with knee osteoarthritis place greater loads on the knee during gait? a preliminary study. Arch Phys Med Rehabil 2005 Apr 1;86(4):703–9.
44. Nisell R. Mechanics of the knee: a study of joint and muscle load with clinical applications. Acta Orthopedica Scandinavica 1985;56(Suppl 216):1–42.
45. Herzog W, Read LJ. Lines of action and moment arms of the major force-carrying structures crossing the human knee joint. J Anat 1993 Apr;182(Pt 2):213–30.

46. Visser JJ, Hoogkamer JE, Bobbert MF, Huijing PA. Length and moment arm of human leg muscles as a function of knee and hip-joint angles. Eur J Appl Physiol Occup Physiol 1990;61 (5–6):453–60.
47. Yamaguchi GT, Zajac FE. A planar model of the knee joint to characterize the knee extensor mechanism. J Biomech 1989;22 (1):1–10.
48. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. J Orthop Res 1991 Jan;9(1):113–9.
49. Neptune RR, Sasaki K, Kautz SA. The effect of walking speed on muscle function and mechanical energetics. Gait Posture 2008 Jul;28(1):135–43.
50. Hubley-Kozey CL, Deluzio KJ, Landry SC, McNutt JS, Stanish WD. Neuromuscular alterations during walking in persons with moderate knee osteoarthritis. J Electromyogr Kinesiol 2006 Aug;16(4):365–78.
51. Wu JZ, Chiou SS, Pan CS. Analysis of musculoskeletal loadings in lower limbs during stilts walking in occupational activity. Ann Biomed Eng 2009 Jun;37(6):1177–89.